

WHAT IS CLAIMED IS:

1           1.    A method of screening a plurality of test  
2    compounds for an effect on a biochemical system, comprising:  
3            providing a substrate having at least a first  
4    surface, and at least two intersecting channels fabricated in  
5    said first surface, at least one of said at least two  
6    intersecting channels having at least one cross-sectional  
7    dimension in a range from 0.1 to 500  $\mu\text{m}$ ;  
8            flowing a first component of a biochemical  
9    system in a first of said at least two intersecting channels;  
10          flowing at least a first test compound from a  
11   second channel into said first channel whereby said first test  
12   compound contacts said first component of said biochemical  
13   system; and  
14          detecting an effect of said at least first test  
15   compound on said biochemical system.

1           2.    The method of claim 1, wherein said at least  
2   first component of a biochemical system produces a detectable  
3   signal representative of a function of said biochemical  
4   system.

1           3.    The method of claim 1, wherein said at least  
2   first component further comprises an indicator compound which  
3   interacts with said first component to produce a detectable  
4   signal representative of a functioning of said biochemical  
5   system.

1           4.    The method of claim 1, wherein said first  
2   component of a biochemical system comprises an enzyme and a  
3   substrate for said enzyme, wherein action of said enzyme on  
4   said substrate produces a detectable signal.

1           5.    The method of claim 1, wherein said first  
2   component of a biochemical system comprises a receptor/ligand  
3   binding pair, wherein at least one of said receptor or ligand  
4   has a detectable signal associated therewith.

1           6. The method of claim 1, wherein said first  
2 component of a biochemical system comprises a receptor/ligand  
3 binding pair, wherein binding of said receptor to said ligand  
4 produces a detectable signal.

1           7. The method of claim 1, wherein said at least  
2 first component of a biochemical system is a biological  
3 barrier and said effect of said at least first test compound  
4 is an ability of said test compound to traverse said barrier.

1           8. The method of claim 7, wherein said barrier is  
2 selected from the group consisting of an epithelial or an  
3 endothelial layer.

1           9. The method of claim 1, wherein said at least  
2 first component of a biochemical system comprises cells, and  
3 said detecting step comprises determining an effect of said  
4 test compound on said cells.

1           10. The method of claim 9, wherein said cells are  
2 capable of producing a detectable signal corresponding to a  
3 cellular function, and said detecting step comprises detecting  
4 an effect of said test compound on said cellular function by  
5 detecting a level of said detectable signal.

1           11. The method of claim 9, wherein said detecting  
2 step comprises detecting an effect of said test compound on  
3 viability of said cells.

1           12. A method of screening a plurality of test  
2 compounds for an effect on a biochemical system, comprising:  
3           providing a substrate having at least a first  
4 surface, and at least two intersecting channels fabricated in  
5 said first surface, at least one of said at least two  
6 intersecting channels having at least one cross-sectional  
7 dimension in a range from 0.1 to 500  $\mu\text{m}$ ;

8 continuously flowing a first component of a  
9 biochemical system in a first channel of said at least two  
10 intersecting channels;  
11 periodically introducing a different test  
12 compound into said first channel from a second channel of said  
13 at least two intersecting channels; and  
14 detecting an effect of said test compound on  
15 said at least first component of a biochemical system.

1 13. The method of claim 12, wherein said step of  
2 periodically introducing comprises flowing a plurality of  
3 different test compounds into said first channel from a second  
4 channel of said at least two intersecting channels, each of  
5 said plurality of different test compounds being physically  
6 isolated from each other of said plurality of different test  
7 compounds.

1 14. The method of claim 12, wherein said at least  
2 first component of a biochemical system produces a detectable  
3 signal representative of a function of said biochemical  
4 system.

1 15. The method of claim 14, wherein said detecting  
2 comprises monitoring said detectable signal from said  
3 continuously flowing first component at a point on said first  
4 channel, said detectable signal having a steady state  
5 intensity, and wherein said effect of said interaction between  
6 said first component and said test compound comprises a  
7 deviation from said steady state intensity of said detectable  
8 signal.

1 16. The method of claim 14, wherein said at least  
2 first component further comprises an indicator compound which  
3 interacts with said first component to produce a detectable  
4 signal representative of a functioning of said biochemical  
5 system.

1           17. The method of claim 16, wherein said first  
2 component of a biochemical system comprises an enzyme and said  
3 indicator compound comprises a substrate for said enzyme,  
4 wherein action of said enzyme on said substrate produces a  
5 detectable signal.

1           18. The method of claim 14, wherein said at least  
2 first component of a biochemical system comprises a  
3 receptor/ligand binding pair, wherein at least one of said  
4 receptor or ligand has a detectable signal associated  
5 therewith.

1           19. The method of claim 18, wherein said receptor  
2 and said ligand flow along said first channel at different  
3 rates.

1           20. The method of claim 14, wherein said first  
2 component of a biochemical system comprises a receptor/ligand  
3 binding pair, wherein binding of said receptor to said ligand  
4 produces a detectable signal.

1           21. The method of claim 12, wherein said at least  
2 first component of a biochemical system comprises cells, and  
3 said detecting step comprises determining an effect of said  
4 test compound on said cells.

1           22. The method of claim 21, wherein said cells are  
2 capable of producing a detectable signal corresponding to a  
3 cellular function, and said detecting step comprises detecting  
4 an effect of said test compound on said cellular function by  
5 detecting a level of said detectable signal.

1           23. The method of claim 21, wherein said detecting  
2 step comprises detecting an effect of said test compound on  
3 viability of said cells.

1           24. A method of screening a plurality of different  
2 test compounds for an effect on a biochemical system,  
3 comprising:

4           providing a substrate having at least a first  
5 surface, and a plurality of reaction channels fabricated in  
6 said first surface, each of said plurality of reaction  
7 channels being fluidly connected to at least two transverse  
8 channels fabricated in said surface;

9           introducing at least a first component of a  
10 biochemical system into said plurality of reaction channels;

11           flowing a plurality of different test compounds  
12 through at least one of said at least two transverse channels,  
13 each of said plurality of test compounds being introduced into  
14 said at least one transverse channels in a discrete volume;

15           directing each of said plurality of different  
16 test compounds into a separate one of said plurality of  
17 reaction channels; and

18           detecting an effect of each of said test  
19 compounds on said at least one component of said biochemical  
20 system.

1           25. The method of claim 24, wherein said at least  
2 first component of said biochemical system produces a flowable  
3 detectable signal representative of a function of said  
4 biochemical system.

1           26. The method of claim 25, wherein said detectable  
2 flowable signal produced in each of said plurality of reaction  
3 channels is flowed into and through said second transverse  
4 channel, each of said detectable flowable signals produced in  
5 each of said plurality of reaction channels being physically  
6 isolated from each other of said detectable flowable signals,  
7 whereupon each of said detectable flowable signals is  
8 separately detected.

1           27. The method of claim 25, wherein said flowable  
2 signal comprises a soluble signal.

1           28. The method of claim 27, wherein said soluble  
2 signal is selected from fluorescent or colorimetric signals.

1           29. The method of claim 24, wherein said at least  
2 first component further comprises an indicator compound which  
3 interacts with said first component to produce a detectable  
4 signal representative of a functioning of said biochemical  
5 system.

1           30. The method of claim 29, wherein said first  
2 component of a biochemical system comprises an enzyme and said  
3 indicator compound comprises a substrate for said enzyme,  
4 wherein action of said enzyme on said substrate produces a  
5 detectable signal.

1           31. The method of claim 24, wherein said at least  
2 first component of a biochemical system comprises a  
3 receptor/ligand binding pair, wherein at least one of said  
4 receptor or ligand has a detectable signal associated  
5 therewith.

1           32. The method of claim 24, wherein said first  
2 component of a biochemical system comprises a receptor/ligand  
3 binding pair, wherein binding of said receptor to said ligand  
4 produces a detectable signal.

1           33. The method of claim 24, wherein said at least  
2 first component of a biochemical system comprises cells, and  
3 said detecting step comprises determining an effect of said  
4 test compound on said cells.

1           34. The method of claim 33, wherein said cells are  
2 capable of producing a detectable signal corresponding to a  
3 cellular function, and said detecting step comprises detecting  
4 an effect of said test compound on said cellular function by  
5 detecting a level of said detectable signal.

1           35. The method of claim 34, wherein said detecting  
2 step comprises detecting an effect of said test compound on  
3 viability of said cells.

1           36. The method of claim 24, wherein each of said  
2 plurality of different test compounds is immobilized upon a  
3 separate bead, and said step of directing each of said  
4 plurality of different test compounds into a separate one of  
5 said plurality of reaction channels comprises:

6           lodging one of said separate beads at an  
7 intersection of said first transverse channel and each of said  
8 plurality of reaction channels; and

9           controllably releasing said test compounds from  
10 each of said separate beads into each of said plurality of  
11 reaction channels.

1           37. An apparatus for screening test compounds for  
2 an effect on a biochemical system, comprising:

3           a substrate having at least one surface;

4           at least two intersecting channels fabricated  
5 into said surface of said substrate, at least one of said at  
6 least two intersecting channels having at least one cross-  
7 sectional dimension in the range from about 0.1 to about 500  
8  $\mu\text{m}$ ;

9           a source of a plurality different test  
10 compounds fluidly connected to a first of said at least two  
11 intersecting channels;

12           a source of at least one component of said  
13 biochemical system fluidly connected to a second of said at  
14 least two intersecting channels;

15           a fluid direction system for flowing said at  
16 least one component within said second of said at least two  
17 intersecting channels and for introducing said different test  
18 compounds from said first to said second of said at least two  
19 intersecting channels;

20           a cover mated with said surface; and

21 a detection zone in said second channel for  
22 detecting an effect of said test compound on said biochemical  
23 system.

1 38. The apparatus of claim 37, wherein said fluid  
2 direction system generates a continuous flow of said at least  
3 first component along said second of said at least two  
4 intersecting channels, and periodically injects a test  
5 compound from said first channel into said second channel.

1 39. The apparatus of claim 37, further comprising a  
2 source of a second component of said biochemical system, and a  
3 third channel fabricated into said surface, said third channel  
4 fluidly connecting at least one of said at least two  
5 intersecting channels with said source of said second  
6 component of said biochemical system.

1 40. The apparatus of claim 39, wherein said fluid  
2 direction system generates a continuous flow of a mixture of  
3 said first component and said second component along said  
4 second of said at least two intersecting channels, and  
5 periodically injects a test compound from said first channel  
6 into said second channel.

1 41. The apparatus of claim 37, wherein said fluid  
2 direction system continuously flows said plurality of  
3 different test compounds from said first into said second of  
4 said at least two intersecting channels, each of said  
5 plurality of different test compounds being separated by a  
6 fluid spacer.

1 42. The apparatus of claim 37, wherein said fluid  
2 direction system comprises:  
3 at least three electrodes, each electrode being  
4 in electrical contact with said at least two intersecting  
5 channels on a different side of an intersection formed by said  
6 at least two intersecting channels; and



7 a control system for concomitantly applying a  
8 variable voltage at each of said electrodes, whereby movement  
9 of said test compounds or said at least first component in  
10 said at least two intersecting channels may be controlled.

1 43. The apparatus of claim 37, wherein said  
2 detection system includes a detection window in said second  
3 channel.

1 44. The apparatus of claim 43, wherein said  
2 detection system is a fluorescent detection system.

1 45. The apparatus of claim 37, wherein said  
2 substrate is planar.

1 46. The apparatus of claim 37, wherein said  
2 substrate comprises etched glass.

1 47. The apparatus of claim 37, wherein said  
2 substrate comprises etched silicon.

1 48. The apparatus of claim 37, further comprising  
2 an insulating layer disposed over said etched silicon  
3 substrate.

1 49. The apparatus of claim 37, wherein said  
2 substrate is a molded polymer.

1 50. The apparatus of claim 37, wherein said at  
2 least one component of a biochemical system comprises an  
3 enzyme, and a substrate which produces a detectable signal  
4 when reacted with said enzyme.

1 51. The apparatus of claim 50, wherein said  
2 substrate is selected from the group consisting of chromogenic  
3 and fluorogenic substrates.

1           52. The apparatus of claim 37, wherein said at  
2     least first component of a biochemical system comprises a  
3     receptor/ligand binding pair, wherein at least one of said  
4     receptor or ligand has a detectable signal associated  
5     therewith.

1           53. The apparatus of claim 37, wherein said first  
2     component of a biochemical system comprises a receptor/ligand  
3     binding pair, wherein binding of said receptor to said ligand  
4     produces a detectable signal.

1           54. An apparatus for detecting an effect of a test  
2     compound on a biochemical system, comprising:  
3             a substrate having at least one surface;  
4             a plurality of reaction channels fabricated  
5     into said surface;  
6             at least two transverse channels fabricated  
7     into said surface, each of said plurality of reaction channels  
8     being fluidly connected to a first of said at least two  
9     transverse channels at a first point in said reaction  
10    channels, and fluidly connected to a second of said at least  
11    two transverse channels at a second point in said reaction  
12    channels, said at least two transverse channels and said  
13    plurality of reaction channels each having at least one cross-  
14    sectional dimension in the range from about 0.1 to about 500  
15    μm;

16             a source of at least one component of said  
17     biochemical system, said source of at least one component of  
18     said biochemical system being fluidly connected to each of  
19     said plurality of reaction channels;

20             a source of test compounds fluidly connected to  
21     said first of said at least two transverse channels;

22             a fluid direction system for controlling  
23     movement of said test compound and said at least one component  
24     within said at least two transverse channels and said  
25     plurality of reaction channels;

26             a cover mated with said surface; and

27 a detection system for detecting an effect of  
28 said test compound on said biochemical system.

1 55. The apparatus of claim 54, wherein said fluid  
2 control system comprises:  
3 a plurality of individual electrodes, each in  
4 electrical contact with each terminus of said at least two  
5 transverse channels; and  
6 a control system for concomitantly applying a  
7 variable voltage at each of said electrodes, whereby movement  
8 of said test compounds or said at least first component in  
9 said at least two transverse channels and said plurality of  
10 reaction channels may be controlled.

1 56. The apparatus of claim 54, wherein each of said  
2 plurality of reaction channels comprises a bead resting well  
3 at said first point in said plurality of reaction channels.

1 57. The apparatus of claim 54, wherein said source  
2 of at least one component of a biochemical system is fluidly  
3 connected to said plurality of reaction channels by a third  
4 transverse channel, said third transverse channel having at  
5 least one cross sectional dimension in a range of from 0.1 to  
6 500  $\mu\text{m}$  and being fluidly connected to each of said plurality  
7 of reaction channels at a third point in said reaction  
8 channels.

1 58. The apparatus of claim 57, wherein said third  
2 point in said reaction channels is intermediate to said first  
3 and second points in said reaction channels.

1 59. The apparatus of claim 58, further comprising a  
2 particle retention zone in each of said plurality of reaction  
3 channels, between said third and said second points in said  
4 plurality of reaction channels.

1 60. The apparatus of claim 49, wherein said  
2 particle retention zone comprises a particle retention matrix.

1           61. The apparatus of claim 49, wherein said  
2 particle retention zone comprises a microstructural filter.

1           62. The apparatus of claim 54, wherein said  
2 plurality of reaction channels comprises a plurality of  
3 parallel reaction channels fabricated into said surface of  
4 said substrate and said at least two transverse channels are  
5 connected at opposite ends of each of said parallel reaction  
6 channels.

1           63. The apparatus of claim 54, wherein said at  
2 least two transverse channels are fabricated on said surface  
3 of said substrate in inner and outer concentric channels, and  
4 said plurality of reaction channels extend radially from said  
5 inner concentric channel to said outer concentric channel.

1           64. The apparatus of claim 63, wherein said  
2 detection system comprises a detection window in said second  
3 channel.

1           65. The apparatus of claim 64, wherein said  
2 detection system is a fluorescent detection system.

1           66. The apparatus of claim 54, wherein said  
2 substrate is planar.

1           67. The apparatus of claim 54, wherein said  
2 substrate comprises etched glass.

1           68. The apparatus of claim 54, wherein said  
2 substrate comprises etched silicon.

1           69. The apparatus of claim 54, further comprising  
2 an insulating layer disposed over said etched silicon  
3 substrate.

1           70. The apparatus of claim 54, wherein said  
2 substrate is a molded polymer.

1           71. The apparatus of claim 54, wherein said at  
2 least one component of a biochemical system comprises an  
3 enzyme, and an enzyme substrate which produces a detectable  
4 signal when reacted with said enzyme.

1           72. The apparatus of claim 71, wherein said enzyme  
2 substrate is selected from the group consisting of chromogenic  
3 and fluorogenic substrates.

1           73. The apparatus of claim 54, wherein said at  
2 least first component of a biochemical system comprises a  
3 receptor/ligand binding pair, wherein at least one of said  
4 receptor or ligand has a detectable signal associated  
5 therewith.

1           74. The apparatus of claim 54, wherein said first  
2 component of a biochemical system comprises a receptor/ligand  
3 binding pair, wherein binding of said receptor to said ligand  
4 produces a detectable signal.